ABSTRACT FACE PAGE

1. **Presenting Author's name: ___Ariel Nikas_____**
2. **Presenting Author's affiliation: _____Emory University_____**
3. **Presenting Author's title: _____Postdoctoral Research Fellow_____**
4. **Presenting Author's email: _____ariel.nikas@emory.edu_____**
5. **Presenting Author's gender (optional): _____female_____**
6. **Presenting Author's race (optional): _____**
7. **Presenting Author's ethnicity (optional): _____**
8. **Presenting Author's affiliation sector: (check one or more)**
    - Academia
    - Industry
    - Federal Employee/Contractor
    - Private Foundation
    - Other: _____
9. **Presenting Author's Career stage: (check one)**
    - K-12 student
    - Undergraduate student
    - Graduate Student
    - Post-doctoral Trainee
    - Young employee (within first 3 year of post-training position)
    - Mid-level employee (3-10 years of post-training position)
    - Senior-level employee (10+ years of post-training position)
    - Other: _____
10. **Website / twitter handle / other public links (optional): ___https://eimsmgroup.github.io___**
11. **Is this the research presented in this abstract supported by IMAG MSM-related U01 funding? Yes**
12. **If the Presenting Author is a trainee, who is the trainee's primary research advisor? ___Veronika Zarnitsyna__**

TRAINEE POSTER AND ORAL PRESENTATION COMPETITONS:

13. **If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Poster Competition*? Yes**

14. **If the Presenting author is a trainee, would the Presenting Author like to enter his/her abstract in the Trainee Oral Presentation Competition**? Yes**

ESTIMATING WANING OF INFLUENZA VACCINE INDUCED IMMUNITY WITH A MULTI-SCALE MODELING APPROACH

[1]Ariel N. Nikas*, [1]Zheng-Rong Tiger Li, [1]Rustom Antia, and [1]Veronika Zarnitsyna*
[1]Emory University, Atlanta, GA, USA
email: ariel.nikas@emory.edu, veronika.i.zarnitsyna@emory.edu

BACKGROUND: Vaccination is still the best way to protect against influenza, and studies in mice show we can achieve a high level of protection but it wanes over time[1]. Although it is unknown how this waning time scale translates from mice to humans, studies of influenza vaccine efficacy (VE) suggest that protection may wane intra-seasonally. Different levels of prior immunity, vaccination distribution timing, and types of data collected (e.g. from matched cohorts, test-negative design, etc.) complicate interpretation of the results when attempting to estimate vaccine efficacy and its waning in humans. Many studies attempt to estimate influenza vaccine efficacy and waning but the results are contradictory. We aim to quantify the accuracy of these estimates.

METHODS: We use a multi-scale model that links within-host and between-host dynamics of influenza in a human population. The within-host scale of the model is built in line with our previously published studies [2,3]. The between-host model is SIR-based. Heterogeneity in prior immunity and vaccination time during a given season as well as the extent of waning of immunity are all important parameters that may affect the interpersonal infection dynamics. We capture these heterogeneities in an agent-based model framework for the spread of influenza infection. With this general framework, we compare the waning of true vaccine efficacy and the vaccine efficacy observed by simulating different vaccination study types analyzed with different statistical techniques and determine the vaccine's effect on transmission and infection.

RESULTS: We simulate four different scenarios: 1) no waning with complete protection, 2) fixed level of leaky protection, 3) waning from 80% to 50% vaccine induced leaky protection, and 4) waning from complete protection to no protection. Each scenario was run one thousand times with a population of 100,000 and consistent initial conditions and parameters with the exception of vaccine-induced protection level and whether or not vaccine protection waned over a two month period. Analyzing our simulated data with the commonly used Cox proportional hazard model and its Schoenfeld residuals shows that in some waning scenarios (see Scenario 3) the statistical model can incorrectly report no waning in some of the simulations. However in simulations with no waning, the vaccine efficacy as would be calculated by an actual study is quite accurate.

CONCLUSIONS: We conclude that certain study designs and statistical techniques may not always accurately capture seasonal waning of the influenza vaccine in humans. We have also found that the system is sensitive to vaccination timing relative to disease introduction and vaccination coverage levels. In cases where there is waning, the hazard model underestimates the true vaccine efficacy (Scenarios 3,4).

Table 1: Cox proportional hazard model used to analyze 4 different scenarios each with 1000 runs for 100,000 people in the population and vaccination coverage of 40%. This statistical method's conclusions were only completely accurate in the case of complete, non-waning vaccine protection.

Scenarios / Results	1) No Waning: 100% Protection	2) No Waning: 80% Protection	3) Waning: 80%-50% Protection	4) Waning: 100% - 0% Protection
Detected Waning (% simulations)	0%	4.7%	93.3%	97.8%
Avg. Estimated VE	100%	81.7%	54%	17.2%

REFERENCES:
1. Coleclough et al. *Scand. J. Of Immunol.* 62: 2005
2. Zarnitsyna et al. *PLoS Pathog.* 12(6): e1005692, 2016.
3. Zarnitsyna et al. *Front. Immunol.* 7(165): 2016.

ACKNOWLEDGEMENTS: NIH grant U01HL139483.